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Consensus Statement

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Reporting guidelines for precision medicine research of clinical relevance: the BePRECISE checklist

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Precision medicine should aspire to reduce error and improve accuracy in medical and health recommendations by comparison with contemporary practice, while maintaining safety and cost-effectiveness. The etiology, clinical manifestation and prognosis of diseases such as obesity, diabetes, cardiovascular disease, kidney disease and fatty liver disease are heterogeneous. Without standardized reporting, this heterogeneity, combined with the diversity of research tools used in precision medicine studies, makes comparisons across studies and implementation of the findings challenging. Specific recommendations for reporting precision medicine research do not currently exist. The BePRECISE (Better Precision-data Reporting of Evidence from Clinical Intervention Studies & Epidemiology) consortium, comprising 23 experts in precision medicine, cardiometabolic diseases, statistics, editorial and lived experience, conducted a scoping review and participated in a modified Delphi and nominal group technique process to develop guidelines for reporting precision medicine research. The BePRECISE checklist comprises 23 items organized into 5 sections that align with typical sections of a scientific publication. A specific section about health equity serves to encourage precision medicine research to be inclusive of individuals and communities that are traditionally under-represented in clinical research and/or underserved by health systems. Adoption of BePRECISE by investigators, reviewers and editors will facilitate and accelerate equitable clinical implementation of precision medicine.

Precision medicine represents an evolution in the long history of evidence-based medicine and healthcare. Spanning disease classifications and risk factor boundaries, precision medicine is underpinned by four key 'pillars' (prevention, diagnosis, treatment and prognosis)[1,2]. The overarching objective of precision medicine is to reduce error and improve accuracy in medical and health recommendations compared with contemporary approaches[3]. Precision medicine solutions should meet or improve on existing standards for safety. They should also be compatible with the individual's preferences, capabilities and needs and tailored to the cultural and societal conditions of the population. Furthermore, precision medicine should be cost-effective and enhance health equity by increasing access to better medical and healthcare practices for the people most in need.

Cardiometabolic diseases are the leading causes of mortality globally[4]. With this burden projected to worsen over the coming decades[5], innovative approaches to disease prevention, diagnosis and treatment are urgently needed. A plethora of precision medicine approaches are being explored in translational and clinical research.

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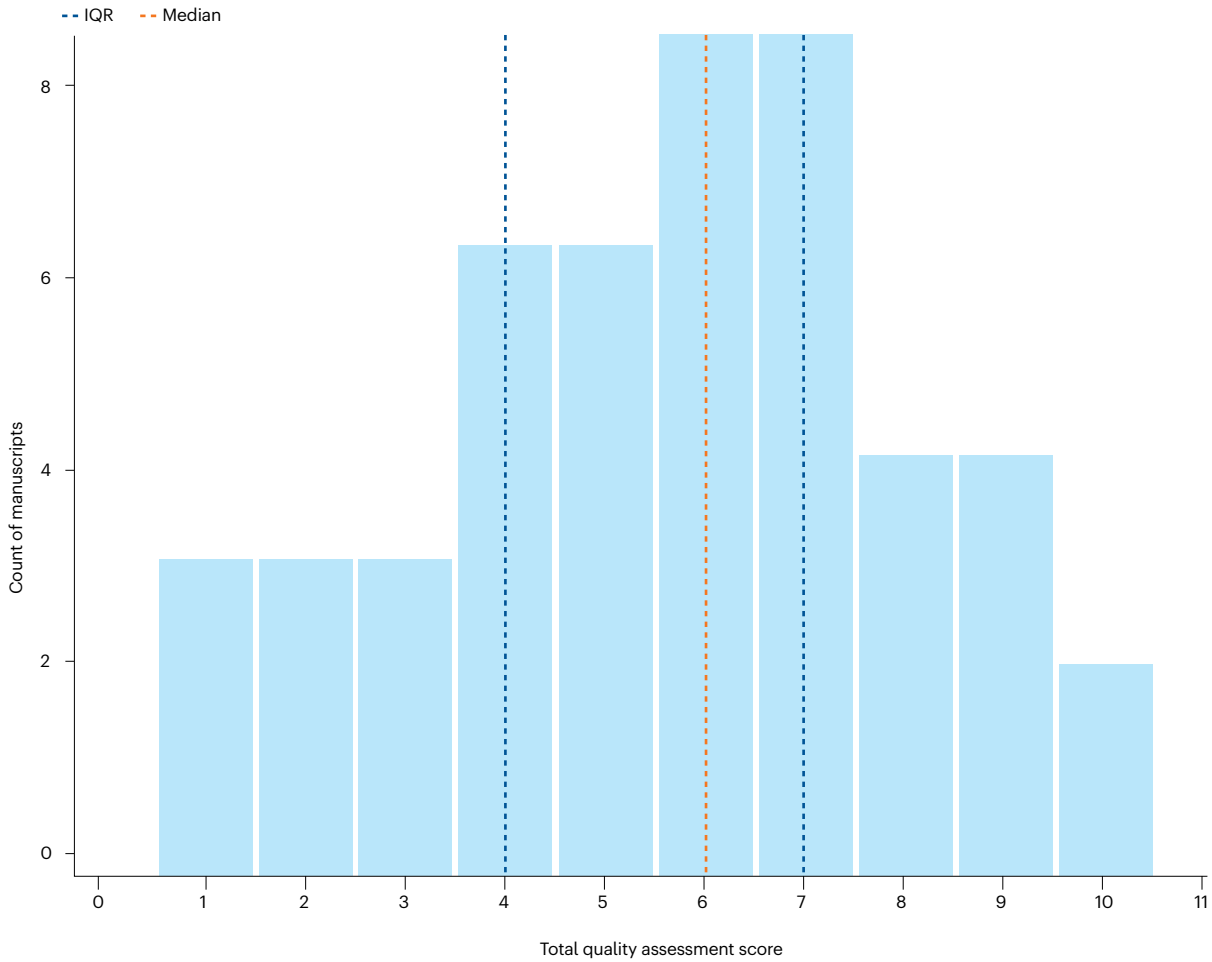

Fig. 1 | Distribution of manuscripts by the total quality assessment scores. Median scores of 47 published precision medicine manuscripts randomly selected for full text review and quality assessment through computer-generated, random-number sequence. IQR, Interquartile range.

However, translating, scaling and implementing these findings for clinical practice have proved difficult. The heterogeneous nature of disease presentation and the etiology of cardiometabolic diseases contribute to these challenges, as does the range and diversity of clinical information, molecular data types and computational analyses used in precision medicine research.

The ability to synthesize data and reproduce research findings are tenets of the modern scientific process, which help maximize progress in evidence-based healthcare and medicine. The 'Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine'[3] was supported by a series of systematic evidence reviews[6–16]. The report focused on key dimensions of precision diabetes medicine, including evidence for prevention, diagnosis, treatment and prognosis in monogenic forms of diabetes, gestational diabetes, and type 1 and type 2 diabetes. A key finding from the report and the systematic evidence reviews underpinning it is that the published literature on precision diabetes medicine lacks evidence standardization or benchmarking against contemporary standards and often overlooks under-represented populations, who tend to bear the greatest burden of diabetes and its complications.

In the present report, we present reporting guidelines for clinically relevant precision medicine research, using common cardiometabolic diseases as the example. We first evaluated a representative sample of the literature on precision medicine in cardiometabolic diseases, determining that the quality of evidence reporting is low, akin to the level previously observed for precision diabetes medicine[3]. We then generated consensus guidelines and a corresponding checklist for reporting of research germane to precision medicine. The purpose of these guidelines is to improve reporting standards so that: (1) evidence can be combined and synthesized in a way that yields meaningful insights from collective efforts; (2) claims of clinical utility can be benchmarked against contemporary standards; and (3) end-user engagement and health equity will be strengthened.

Results

Scoping review

The literature search focused on identifying precision medicine publications using the term 'precision medicine' and associated proxy nomenclature, among other keywords and phrases (Supplementary Methods). The search identified 2,679 publications, of which 13 were excluded owing to duplication. The remaining 2,666 papers were screened, of which 47 were randomly selected (through computer-generated, random-number sequence) for full text review and quality assessment. The summary (count and percentage) of each quality assessment item across all papers and the quality assessment results for each paper are shown in Supplementary Tables 2 and 3. This quality assessment yielded a median score of 6 (interquartile range = 4–7) with none of the papers achieving a positive quality evaluation across all 11 items (Fig. 1).

A summary of the itemized evidence reporting quality is shown in Supplementary Table 2. Most abstracts (81%) reported findings relevant to the four pillars of precision medicine (prevention, diagnosis, treatment and/or prognosis) and provided sufficient detail in the methods sections to determine whether the study was designed to test hypotheses on precision medicine (77%), details about participant eligibility

(75%) and descriptions of standard reporting definitions (70%). The items that were less frequently reported were the description of patient and public involvement and engagement (PPIE) in determining the impact and utility of precision medicine (15%), the inclusion of the term 'precision medicine' in the title or abstract (17%), the reporting of measures of discriminative or predictive accuracy (23%), the description of the approach used to control risk of false-positive reporting (28%), the reporting of effect estimates with 95% confidence intervals and units underlying effect estimates (57%) and the reporting of a statistical test for comparisons of subgroups (for example, interaction test) (60%).

Stakeholder survey

Delphi panel demographics. Of the 23 Delphi panelists, 22 (96%) completed Delphi survey 1, 18 (78%) and attended the full-panel consensus meeting and 22 (96%) completed Delphi survey 2. All panelists engaged in further extensive dialog around key topics through online communication.

Delphi results. The initial checklist in Delphi survey 1 contained 68 items. After Delphi survey 1 and the full-panel consensus meeting, 2 items were added, resulting in 70 items in Delphi survey 2. At the Consensus meeting, it was determined that the checklist should be used together with existing relevant checklists. These include the CONSORT (Consolidated Standards of Reporting Trials)[17] and STROBE (Strengthening the Reporting of Observational Studies in Epidemiology)[18] checklists for interventional trials and observational studies, respectively. This led to a recommendation to remove items covered in established checklists (Supplementary Fig. 1). The scoring from Delphi survey 1, Delphi survey 2 and notes from the Consensus meetings are as shown in Supplementary Table 4. After Delphi survey 2, the consensus was to retain 25 items across 6 core categories.

Guidelines finalization

The executive oversight committee reviewed the panel scores and free-text comments from all the rounds of Delphi surveys to determine the final checklist items and wording. The group discussed five items with inconsistent consensus (between 70% and 80% consensus), resulting in the removal of one item because it overlapped conceptually with another item (17b and 17g in Supplementary Table 4). It was also determined that 'health equity' should be included as an overarching theme, thereby encouraging users of the checklist to consider this topic more broadly when describing precision medicine research. This resulted in removal of two items.

The final checklist comprised 23 items that the executive oversight committee concluded are unique and essential for reporting standards in precision medicine. The final BePRECISE checklist is presented in Table 1, with a downloadable version of the checklist available online (https://www.be-precise.org, and https://www.equator-network.org/reporting-guidelines/).

Explanation of checklist Items

The checklist and the explanation of each item are presented in Table 1. The BePRECISE checklist is intended to complement existing guidelines such as CONSORT[17], STROBE[18] and PRISMA (Preferred Reporting System for Systematic Reviews and Meta-Analyses)[19].

These reporting guidelines use the terms 'precision medicine' and 'personalized medicine' as defined in the 'Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine'[3], as follows:

> 'Precision medicine focuses on minimizing errors and improving accuracy in medical decisions and health recommendations. It seeks to maximize efficacy, cost-effectiveness, safety, access for those in need and compliance compared with contemporary evidence-based medicine. Precision medicine emphasizes tailoring diagnostics or therapeutics (prevention or treatment) to subgroups of populations sharing similar characteristics.'
>
> Personalized medicine refers to 'the use of a person's own data to objectively gauge the efficacy, safety, and tolerability of therapeutics, and, subjectively, to tailor health recommendations and/or medical decisions to the individual's preferences, circumstances, and capabilities'.

Accordingly, personalized medicine can be viewed as being nested within the broader concept of precision medicine.

Equity and PPIE (E1–E4). Equity, diversity and inclusivity considerations and the involvement of patients and public is a crosscutting theme in this checklist. Where relevant, papers should include a description of how equity has been considered, including diversity and inclusivity of study participants, and whether there was PPIE. Cohort selection biases and probable risks when extrapolating the study's results to other populations should be clearly described.

The selection of participants should consider racial, ethnic, ancestral, geographic and sociodemographic characteristics[20], and include an explanation for the inclusion or exclusion of groups that are typically under-represented in clinical research (E1 and E2). Race and ethnicity are social constructs but, as they are categories recognized by some government and health authorities in contexts that are relevant to precision medicine, we have elected to retain inclusion of these somewhat controversial terms here.

PPIE in any part of the study should be described, including but not limited to design, conduct and reporting (E3).

Where possible, and ideally with guidance from those with lived experience, the potential impact of the research findings on the target population(s) should be discussed (E4). Consider co-writing these aspects with PPIE representatives.

Title and abstract (1.1–1.4). In the title and/or abstract, the term 'precision medicine' should be included to highlight that the research is relevant to precision medicine (1.1). Given that precision medicine is an approach that can be used in several research contexts, the study design (for example, randomized clinical trial (RCT), retrospective observational) and the research question should be stated clearly (1.2). Use of the terms 'prevention', 'diagnostics', 'treatment' or 'prognostics' is needed to highlight which pillar of precision medicine the study concerns[3] (1.3). To ensure transparency about generalizability and/or applicability of the findings to a specific population or subgroup, the study population must be described (1.4).

Background and objectives (2.1–2.2). The background should clearly describe the rationale for the chosen precision medicine approach, including the context and prior work that led to it and the specific hypothesis being tested (2.1). To provide the reader with greater context, papers should also state the nature and objective of the precision medicine study as 'etiological', 'discovery', 'predictive' and/or 'confirmatory' (2.2).

Methods (general). Although this reporting guide focuses on clarifying elements of papers that are germane to precision medicine, authors are strongly encouraged to ensure that methods also adhere to other appropriate reporting guidelines (for example, CONSORT and STROBE), with the overarching goal of ensuring that the study protocol described therein could, in principle, be accurately reproduced by third-party investigators.

Methods (3.1–3.7). Methods should describe the aspects of a study design relating to precision medicine in such detail that the design can be understood and replicated (3.1). The rationale for the choice of primary outcome should be clearly stated (3.2).

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Table 1 | BePRECISE reporting guidelines for precision medicine research

Item number	Item wording	Elaboration and explanation of item
E. Equity, inclusion, diversity and PPIE. Authors are encouraged to address these topics in their manuscripts within relevant sections. The reporting items listed herein are not exhaustive and all considerations of PPIE (including patient-reported outcomes and experience), as well as any community engagement efforts, should be described wherever possible		
E1	Use appropriate population descriptors such as ancestry, geographic and sociodemographic characteristics of all participants, particularly those in under-represented groups	In cases where data from under-represented group(s) are collected and the subsample size is $n \geq 20$, all data should be analyzed and reported (even in cases where subgroup analyses might be considered underpowered, because this will facilitate subsequent meta-analyses of results). A minimum sample size of 20 is based on the 'All of Us Research Program Data User Code of Conduct' (https://www.researchallofus.org/faq/data-user-code-of-conduct) and is intended to avoid disclosing individual participant identity Avoid merging subgroups into larger heterogeneous groups (for example, 'non-European ancestry') Although there is ongoing discussion on the appropriate use of words and terms describing groups within populations, this checklist yields to other guidelines on this matter. If data pertaining to race and/or ethnicity are collected this should be reported in accordance with relevant established guidance
E2	Describe the implications of inclusion and/or exclusion of people who are understudied in precision medicine research or underserved by health services	Describe implications for successful extrapolation of study findings to other groups, particularly those typically under-represented in precision medicine research
E3	Describe PPIE in any aspect of the study design, conduct and/or reporting	PPIE may include consultation, involvement, partnership or leadership by end-users, including being part of the research and/or authorship team
E4	Where possible, and ideally with guidance from PPIE representatives, describe the potential impact of the study's results from a lived-experience perspective, especially the impact of the research on people living with disease	
1. Title and/or abstract		
1.1	Include 'precision medicine' in the title or abstract	These reporting guidelines use the terms 'precision medicine' and 'personalized medicine', defined elsewhere[3], as follows: 'Precision medicine focuses on minimizing errors and improving accuracy in medical decisions and health recommendations. It seeks to maximize efficacy, cost-effectiveness, safety, access for those in need and compliance compared with contemporary evidence-based medicine. Precision medicine emphasizes tailoring diagnostics or therapeutics (prevention or treatment) to subgroups of populations sharing similar characteristics. 'The use of a person's own data to objectively gauge the efficacy, safety, and tolerability of therapeutics, and, subjectively, to tailor health recommendations and/or medical decisions to the individual's preferences, circumstances, and capabilities.'
1.2	State the research question and study design	'Study design' refers to the specific type of clinical trial design (for example, parallel arm, randomized crossover, recall-by-genotype) or observational cohort design (for example, cross-sectional study, prospective cohort study, case–cohort study, case–control study). If the study design involves time-series assessments this should also be highlighted
1.3	Describe whether the study relates to prevention, diagnostics, treatment and/or prognostics	
1.4	Describe the population or subgroup that is the focus of the current analysis	
2. Background and objectives		
2.1	State the study hypothesis describing the specific rationale for the precision medicine approach	
2.2	State the study objective(s) of the precision medicine study as (a) etiological, (b) discovery, (c) predictive and/or (d) confirmatory. State all that apply. See the explanation and elaborations document for detailed descriptions of the objectives	(a) Etiological: characterization of heterogeneity across individual-level data (b) Discovery: exploration of associations between a set of clinical features and outcome heterogeneity (for example, descriptive RCT subgroup analysis or exploratory analysis of risk factors) (c) Predictive: development of a specific approach(es) to predict heterogeneity in clinical or treatment-related outcomes for individuals or subgroups (d) Confirmatory: reproduction of a previously proposed precision medicine approach
3. Methods		
3.1	Describe aspects of the study design relevant to precision medicine that are necessary for the design to be adequately understood by the reader	
3.2	Provide the rationale for choice of outcome(s)	
3.3	If the dataset is a subset of a larger study, describe how and why the subset(s) of participants used in the analysis was selected	
3.4	Define any markers used for stratification or prediction of outcomes in individuals or subgroups	'Markers' in this context could include (and not be limited to) biomarkers, molecular markers and clinical characteristics, as well as societal, economic, geographic and cultural factors

Table 1 (continued) | BePRECISE reporting guidelines for precision medicine research

Item number	Item wording	Elaboration and explanation of item
3.5	Provide details of any measures taken to mitigate type 1 and/or type 2 error. Describe a priori power calculations and adjustment for multiple testing, if performed	
3.6	Describe any approach used for internal and/or external replication and/or validation and whether these analyses were planned and relevant datasets identified before or after conclusion of primary analyses	'Replication' analyses are those that seek to directly reproduce primary analyses. 'Validation' analyses are those that seek to generate results using orthogonal methods to those used in the primary analyses that strengthen its conclusions
3.7	Specify how the sample size for any replication/validation study was determined	
4. Results		
4.1	Specify the number of participants in each analysis and provide baseline characteristics	If analysis includes comparison of subgroups, baseline characteristics for each subgroup should be provided
4.2	Report statistical tests and results for subgroup comparisons	Comparisons between subgroups should include appropriate test statistics, which may include tests of interaction and heterogeneity, and in cluster analyses tests of probability for cluster assignment (for example, relative entropy statistic)
4.3	If benchmarking against current practice was undertaken, describe these results. State if benchmarking was not performed	Provide formal comparisons against current practice to assess performance of the precision medicine approach. For example, for prediction models, compare new biomarkers with established prediction variables, formally testing differences in prediction performance. For treatments, compare measures of clinical effectiveness (for example, number needed to treat) between new and conventional approaches. If such comparisons are not possible, provide an explanation
4.4	Provide results for all attempted validation and/or replication analyses	
5. Discussion		
5.1	General limitations	Describe how study characteristics or analytical methods may introduce bias, particularly as these pertain to features of the analysis related to precision medicine (for example, subgroup comparisons)
5.2	Interpretation: describe the precision medicine approach that could potentially be applied in clinical practice	

To enable readers to assess bias and interpret the study findings, this section should state how the participants were identified and enrolled in the study (4.1) and (if applicable) how a subset of a broader group of participants was selected from an existing study (3.3). Any markers used for stratification or prediction should be explicitly stated with an explanation of how the marker(s) was(were) chosen (3.4).

The sample size and how it was derived should be described, for example, following a priori power calculations, or if the sample size was limited primarily by availability or cost, and any implications that this might have for type 2 error (3.5). Authors should also describe attempts to minimize false-positive discovery, especially when multiple testing has occurred (3.5).

If any replication and/or validation analyses were undertaken, a clear description should be given of the approach, including whether these analyses were planned and relevant datasets identified before or after conclusion of primary analyses (3.6), in addition to justification for the sample size and choice of replication cohort (3.7).

Results (4.1–4.4). The number of participants in the study should be provided, along with a table of baseline characteristics (4.1). If the analysis involves comparison (rather than discovery) of subgroups, the baseline characteristics and numbers of participants should be provided by the subgroup.

Results from any statistical tests done should be reported. Any comparisons of subgroups should include appropriate test statistics, which may include tests of interaction and heterogeneity, and in cluster analyses tests of probability for cluster assignment (for example, relative entropy statistic) (4.2).

Key findings should be benchmarked against current reference standards or practice, if they exist, so that the reader can determine the likely benefit of translating the study's findings into clinical practice. This may include, for example, the comparison of the new and existing approaches using tests of discriminative (cross-sectional) or predictive (prospective) accuracy, or estimation of net reclassification or changes in numbers needed to treat. If benchmarking has not been done, a clear explanation should be given (4.3).

If validation and/or replication analyses were undertaken, the results of all such attempts at analyses should be clearly described (4.4).

Discussion (5.1–5.2). The paper should include a balanced and nuanced discussion of any limitations to the interpretation and/or implementation of the reported findings. The limitations section should consider biases that might prevent fair and equitable generalization of the study's findings to other populations, particularly to groups that are under-represented within the published literature. Authors are also encouraged to consider other potential biases that might arise with stratified and subgroup analyses (5.1).

If there is a direct clinical implication of the study's findings, authors should describe how their findings might be applied in clinical practice. This might, for example, include an explanation of how any algorithms, technologies or risk markers that stem directly from the research might benefit clinical practice.

Discussion

The BePRECISE guidelines are intended to enhance publication of research on precision medicine by improving quality and standardization of reporting. In turn, it is anticipated that this will help improve

and accelerate the impact of precision medicine research on the health and well-being of target populations and individuals.

BePRECISE was initiated to follow up on recommendations from the 'Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine'[3]. The report, founded on 16 systematic evidence reviews summarizing research described in >100,000 published papers, found a low degree of standardization across the published literature, with a broad absence of key information needed for benchmarking against contemporary standards, validation analyses and meaningful interpretation of research findings.

Implementation of the checklist

These reporting guidelines were derived through structured evaluation and consensus processes undertaken by subject-matter experts in precision medicine for complex traits. The report is premised on cardiometabolic disease translational research but is relevant to translation of research in other complex diseases. These guidelines are directed toward authors describing translational research in precision medicine, as well as for journal editors handling submissions in this field. These guidelines may also be of value to funding agencies, policy advisers and health educators.

The BePRECISE guidelines are designed to be used together with existing study-specific checklists such as CONSORT[17], STROBE[18] and STORMS (Strengthening the Organization and Reporting of Microbiome Studies)[21]. Publications relevant to precision medicine cover diverse topics and study designs; thus, to accommodate this diversity, we recommend that authors elaborate on relevant details related to checklist items to facilitate manuscript evaluations by journal editors and peer reviewers who will determine whether a given paper has addressed the BePRECISE checklist criteria.

Health equity

Precision medicine has the potential to improve health equity by making health advice and medical therapies more accessible to those in most need and by being more effective and acceptable to the recipient than contemporary clinical approaches. Nevertheless, as the 'inverse care law'[22] highlights, the best healthcare often reaches those who need it least. We believe that precision medicine research should place emphasis on the development of solutions for people in greatest need, regardless of who or where they are.

Ensuring representation of underserved populations, where the disease burden can be high, is important because determining the effectiveness of precision medicine solutions requires data from the target populations. Research in population genetics provides clear evidence of this, where the predictive accuracy of polygenic burden scores can be low when applied outside the data-source population, even when these populations are geographically proximal[23,24]. Raising awareness of these challenges by discussing them in the health literature and, ultimately, by addressing them through improved study design could facilitate enhancement of health equity using precision medicine approaches.

Promoting equity through precision medicine requires awareness of the many biases. For this reason, the BePRECISE guidelines place emphasis on equity, diversity and inclusion as an overarching concept throughout the checklist.

PPIE

As with health equity, the BePRECISE guidelines position PPIE as a crosscutting theme to motivate its consideration in all elements of precision medicine translational research. We encourage those using the BePRECISE checklist to follow existing guidance on PPIE[25]. Ensuring that the eventual recipients of precision medicine solutions are adequately represented in the planning, execution and reporting of precision medicine research will help maximize the translational value of the research. Ideally, research teams should include members of the communities that will eventually benefit from this work, including in leadership roles, although to achieve this will often require long-term capacity strengthening. This engagement will help ensure that the relevance and utility of the research output are maximized. It will also strengthen the potential for target populations to determine their own health trajectories. Where this is not immediately achievable, establishing authentic partnerships with representatives from these target populations should be prioritized. This may involve community consultations, training opportunities and co-creation of research proposals with assigned community members, through dissemination and translation of research findings. Moreover, the selection of study participants should be done equitably and result in study cohorts that are representative of the populations who are the focus of the research[26]. The use of patient-reported outcome measures and patient-reported experience measures should be considered during the research design and execution phases, and reported in research papers wherever possible following established guidelines[27,28]. Doing so will amplify the patient voice and maximize the relevance of the research to the target populations and individuals.

Cost-effectiveness

The translation of precision medicine research into practice will invariably depend on it being cost-effective, affordable and accessible. This initial version of the BePRECISE checklist does not include checklist items pertaining directly to these important factors. The consensus view was that such analyses are sufficiently complex to stand alone and are likely to be outside the scope of most current precision medicine research. This topic may be revisited in subsequent versions of the checklist.

Strengths and limitations

We believe that implementation of the BePRECISE checklist in the context of academic publishing will strengthen standardization of reporting across precision medicine research, ultimately enabling improved and equitable translation of research findings into the clinical and public health settings. The checklist will also encourage investigators to improve study design, particularly with respect to health equity. Other strengths include rigor of our consensus methods and the diverse range of societal backgrounds and expertise of our group.

We acknowledge that precision medicine in many complex diseases is relatively nascent (with the exception of precision oncology), with the needs of the field and stakeholders evolving. We plan to evaluate uptake of the checklist among journals and authors to assess whether items should be added or removed from the checklist as the field matures. An additional limitation is that the BePRECISE consensus group is small by comparison with similar efforts in other fields of research. We will involve a larger group of experts with broader global and technical representation in future efforts, including increased representation from low- and middle-income countries and individuals with more diverse lived experiences. Additional technical expertise may also be needed from other disciplines, including health economics and health systems administration, for example.

We acknowledge that journal formatting requirements and procedures may not always entirely align with the checklist specifications. We removed a checklist item for provision of a plain language summary, for example, because many journal formats are presently unable to accommodate this type of additional material. However, we hope that in the future editors and publishers of medical and scientific journals will include space for this incredibly important component that facilitates scientific communication with the public.

We defer to editorial and reviewer discretion in implementation of the BePRECISE checklist. Although the BePRECISE checklist items are included to support best scientific practices, at least in the short term, some ongoing precision medicine studies will not have addressed the

health equity or PPIE considerations in their design. We do not expect that insufficient attention to these items would be a sole reason for not considering a manuscript for review, unless blatant disregard for participant and/or community safety, privacy or respect has occurred in the study design and/or conduct. Over time, however, we hope that health equity and PPIE will be considered as standard practice in precision medicine research and implementation.

Conclusions

The BePRECISE reporting guidelines have been generated through a structured consensus process to address the need for better reporting of clinical translational research in precision medicine in common complex diseases. The burgeoning literature on this topic is reported inconsistently, impeding the assimilation, syntheses and interpretation of evidence. There is a general lack of benchmarking against contemporary standards, a situation that makes it impossible to determine whether new precision medicine approaches might be beneficial, feasible and sustainable. Moreover, very little existing precision medicine research has incorporated PPIE or focused on the groups within societies most in need of innovative precision medicine solutions. These barriers limit the positive impact that precision medicine could have on the health and well-being of those most in need. The BePRECISE reporting guidelines are intended to help address these and other important challenges.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-024-03033-3.

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Methods

Consortium structure

The BePRECISE Consortium comprised an executive oversight committee (S.S.L., Z.S.-A., M.L.M., A.H.N., S.S.R., J.L.S. and P.W.F.), which oversaw the full process, with representation across key domain areas, and an evidence evaluation group (Z.S.-A., M.L.M., A.A., H.F., M.-F.H., M.F.G., J.M., D.K.T., M.I.T., S.S.R., J.L.S. and P.W.F.), which undertook the scoping review to determine current reporting standards. All consortium members participated in a Delphi consensus process[29]. The Consortium chair and co-chair were P.W.F. and S.S.L., respectively (Supplementary Table 1).

Protocols and registrations

A scoping review protocol was developed before initiating the literature review or consensus activities and was registered in the Open Science Framework (http://osf-registrations-nh4g2-v1). The consensus process followed the EQUATOR (Enhancing the QUAlity and TRansparency of health Research) Network recommendations for reporting guidelines development (https://www.equator-network.org/library/equator-network-reporting-guideline-manual) and was registered with EQUATOR as 'Reporting guidelines under development' (https://www.equator-network.org/library/reporting-guidelines-under-development/reporting-guidelines-under-development-for-other-study-designs). The final BePRECISE guidelines are available on the Equator website (https://www.equator-network.org/reporting-guidelines/).

Scoping review

The purpose of the scoping review was to determine whether the published literature on precision medicine in cardiometabolic diseases met a minimum threshold for reporting quality. We set the minimum expectation as a condition where most (that is, ≥50%) published papers in this domain are adequately reported. To define a study as adequately or inadequately reported (as a binary variable), members of the scoping review committee identified, through consultation, 11 key items (Supplementary Tables 2 and 3). Papers that met all 11 reporting criteria were deemed, a priori, to be adequately reported.

The checklist items used to assess the reporting quality of studies captured in the scoping review were determined before the Delphi surveys were undertaken. These scoping review checklist items correspond with some of those used in the Delphi surveys that formed the basis of the final BePRECISE checklist, because both the scoping review and Delphi surveys are, to varying degrees, derived from the findings of the 'Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine'[3]. The scoping review was intended to provide a snapshot of the quality of reporting in a subset of literature relating to precision medicine. It was not undertaken to inform the items in the BePRECISE checklist; this purpose was served by the systematic evidence reviews[6–16] and the Consensus report[3] described above.

Based on the findings of the precision diabetes medicine Consensus report[3], we hypothesized that no more than 30% of currently published studies are adequately reported. This assumption was tested by full text reviewing a statistically powered, random subsample of published papers on precision medicine across cardiometabolic diseases ('Search strategy' and 'Sample size estimation'). This scoping review was conducted in accordance with the PRISMA Extension for Scoping Review guidelines[30] to identify and assess the current literature on precision medicine in cardiometabolic diseases and was completed before the 'guidelines consensus process' described below.

Sample size estimation. The literature search was not intended to be a comprehensive evaluation of the published evidence, but instead to provide an unbiased representation of this literature. To determine how many papers should be reviewed as a representative sample of the published literature, an a priori sample size calculation was performed using SAS software v.9.4 (SAS Institute). Given the scenario described, we used a two-sided test with a type 1 error threshold (critical α) of 0.05, assuming a null hypothesis proportion of 0.50, which corresponds to our minimum expectation, an expected number of adequately reported papers of <30% and nominal power of 80%. This calculation determined that 47 randomly selected papers should be full text reviewed to ascertain whether the assumed proportion of adequately reported studies is significantly lower than the prespecified null proportion (that is, to infer that the quality of papers reported in this field is lower than the minimum expectation).

Search strategy. We searched the PubMed database (https://pubmed.ncbi.nlm.nih.gov) to identify relevant articles published in the past 5 years (January 2019 to January 2024). The search strategy incorporated keywords and terms (https://www.ncbi.nlm.nih.gov/mesh) in human epidemiological cohorts and clinical trials representing: (1) precision medicine, (2) cardiometabolic diseases and (3) clinical translation (see Supplementary Methods for the detailed search strategy). The search was constrained to publications written in English. Conference abstracts, case reports, study protocols, reviews and animal studies were excluded.

Study selection and quality assessment. Covidence software (https://www.covidence.org; Veritas Health Innovation) was used to manage the scoping review selection process. Studies were filtered in three stages: (1) removal of duplicate publications; (2) ascertainment of study eligibility based on title and abstract by at least two independent reviewers; and (3) full text review of 47 randomly selected studies, where at least 2 independent reviewers assessed the eligibility of each publication according to the inclusion and exclusion criteria. Each paper was further evaluated to determine whether it met the 11 predetermined quality criteria. Any conflicts were subsequently resolved by an independent reviewer.

Consensus process

The five-step consensus process was based on a modified Delphi and nominal group technique[29]. The consensus process involved: (1) completion of an initial Delphi survey (6–13 February 2024); (2) a consensus meeting (15–16 February 2024); and (3) a second Delphi survey (19–26 February 2024). Finalization of the checklist was conducted at a second consensus meeting by the executive oversight committee (5–6 March 2024), who reviewed the voting of all rounds of the Delphi survey, made final decisions about item inclusion and refined wording of the BePRECISE checklist. The executive oversight committee also evaluated the checklist against two publications on precision medicine determined through the scoping review to be of high and low quality, respectively. The final version of the checklist was circulated to all panel members for consultation and approval (13–19 March 2024).

The items in the first iteration of Delphi survey 1 were derived from existing checklists: CONSORT[17], STROBE[18], CONSORT-Equity 2017 extension[31] and STrengthening the REporting of Genetic Association Studies (STREGA)—an extension of the STROBE guidelines[32]. Additional items specific to precision medicine were generated based on the reporting gaps identified from the series of systematic reviews (11 published) that underpinned the 'Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine'[3]. The draft of Delphi survey 1 was presented to the full panel at a roundtable discussion followed by co-development with the full panel through an online document-sharing platform. The final items for Delphi survey 1, including the input sources for its development, are shown in Supplementary Table 3.

The Delphi survey response scale had five options: 'Completely inappropriate', 'Somewhat inappropriate', 'Neither appropriate nor inappropriate', 'Somewhat appropriate' and 'Completely appropriate'. The consensus threshold was defined a priori as at least 80% of the panel

voting for 'Completely appropriate' or 'Somewhat appropriate'. Items with voting scores under this consensus threshold were discussed at the Consensus meetings. The Delphi surveys were administered online and were anonymous. Panelists were invited to provide free-text comments to suggest new items (survey 1 only), suggest a change of wording for a given item or justify their voting decision. The voting scores and anonymous comments for each item from the previous consensus round were provided to panelists at the subsequent rounds, such that consensus was reached iteratively.

Delphi panel and executive oversight committee. The BePRECISE checklist panelists cover the core areas of expertise outlined in the EQUATOR Network recommendations for reporting guidelines development (https://www.equator-network.org/library/equator-network-reporting-guideline-manual). The panel includes subject-matter experts across relevant disease areas and with expertise in the topics highlighted as gaps in the 'Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine'. Moreover, the BePRECISE panelist selection focused on ensuring diversity: (1) global representation (Europe, North America, sub-Saharan Africa and Australia); (2) career stages (23% early career researchers within 10 years of research experience, 27% of mid-career researchers of 11–15 years of experience and 50% of senior researchers of >20 years of experience); and (3) gender (55% of authors being female).

Accordingly, the Delphi panel comprised subject-matter experts in key cardiometabolic disorders (diabetes, obesity, cardiovascular disease, fatty liver disease, renal disease), statistics, study design (epidemiologists and clinical trialists), journal editorial, lived experience, benchmarking and technology, education and translation, health equity, community engagement and clinical practice. Several of these experts are based in or have worked extensively with investigators in low- and middle-income countries (M.R., N.S., J.L.S. and P.W.F.).

The executive oversight committee for this report consisted of multidisciplinary experts in cardiometabolic disorders, equity research, medical journal editorial and lived experience (P.W.F., S.S.L., S.S.R., J.L.S., A.H.N., Z.S.A. and M.L.M.).

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Author contributions

S.S.L. (co-chair), Z.S.-A., M.L.M., A.H.N., S.S.R., J.L.S. and P.W.F. (chair) formed the executive oversight committee. Z.S.-A. (lead), M.L.M., A.A., H.F., M.-F.H., M.F.G., J.M., D.K.T., M.I.T., S.S.R., J.L.S. and P.W.F. formed the evidence evaluation group. S.S.L. (lead), Z.S.-A., M.L.M., A.A., H.F., J.B., C.C., J.M.D., C.L., R.J.F.L., M.M., M.R., A.J.S., N.S., M.-F.H., M.F.G., J.M., D.K.T., M.I.T., A.H.N., S.S.R., J.L.S. and P.W.F. formed the consensus review panel. A.H.N. and C.C. were the PPIE representatives. S.S.L., Z.S.-A., M.L.M., A.H.N., S.S.R., J.L.S. and P.W.F. wrote the first draft of the manuscript. All the authors edited and approved the final version of the manuscript before submission for journal review.

Competing interests

M.L.M. has consulted for and/or received speaker honoraria from Amarin, Amgen, AstraZeneca, Boehringer Ingelheim, Daichi, Eli Lilly, Merck Sharp & Dohme, Novo Nordisk, Novartis and Servier. In the past 5 years, A.H.N. has received an investigator-initiated grant from Abbott Diabetes Care and consulting honoraria from Roche Diabetes Care, Australia and the Australian Diabetes Educators Association. There are no perceived conflicts from previous involvements on this work. C.C. is a member of the Board of Directors for the Steno Diabetes Center in Copenhagen, Denmark. The views expressed in this paper do not necessarily reflect those of the Steno Center. M.R. is a consultant on the Genentech. 'One Roche: Race, Ethnicity and Ancestry ("REA") Initiative'. A.J.S. received research grants (paid to the institution) from: Intercept, Lilly, Novo Nordisk, Echosense, Boehringer Ingelhiem, Pfizer, Merck, Bristol Myers Squibb, Hanmi, Madrigal, Galmed, Gilead, Salix and Malinckrodt; was a consultant for Intercept, Gilead, Merck, NGM Bio, Terns, Regeneron, Alnylam, Amgen, Genentech, Pfizer, Novo Nordisk, AstraZeneca, Salix, Malinckrodt, Lilly, Histoindex, Path AI, Rivus, Hemoshear, Northsea, 89Bio, Altimmune, Surrozen and Poxel; and had ownership interests in Tiziana, Durect, Exhalenz, GENFIT, Galmed, Northsea and Hemoshear. N.S. has consulted for and/or received speaker honoraria from Abbott Laboratories,

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Additional information

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